

Remarks

To address the Examiner's objection to the disclosure, Applicants have amended specification to conform with the suggested guidelines for the specification provided by the Examiner. Section headings have been inserted and the figure descriptions at page 30 line 20 through page 31 line 27 have been deleted from their original location in the specification, modified to add the word "Figure" as appropriate for clarity and inserted, with the appropriate section heading at page 4 after line 22. In addition, an amendment has been made to correct a typographical error. The word "throughout" was erroneously written as "throught", and the specification has been amended to corrected the inadvertent error. In addition, claims 39, 42, 43, 209, 212, and 213 have been amended to add the term "weight/volume". Support for this amendment can be found at least at page 20, lines 21-26 and based on teaching of the specification as a whole. No new matter has been added.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 39, 42, 43, 209, 212, and 213 under 35 U.S.C. §112 second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. The Examiner asserts that the percentage terms in the claims are indefinite as not defined in the claims.

Applicants submit that it would be obvious to one of ordinary skill in the art that the percentages are determined in terms of weight per volume of the water soluble polymer and the medium. The preferred types of the water soluble polymer are described on page 20, lines 23 and 24 as including carboxymethyl cellulose, polyethylene glycol, (especially PEG8000), and low melting point agarose, each of which is a solid. Thus, it would be understood by one of ordinary skill in the art that a percentage of polymer in liquid medium would be a percentage in terms of weight of polymer per volume of medium. Although Applicants respectfully submit that the claim 39, 42, 43, 209, 212, and 213 are not indefinite, Applicants have amended the claims to include the term: weight/volume to increase their clarity.

In view of the foregoing amendments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 39, 42, 43, 209, 212, and 213 under 35 U.S.C. §112 second paragraph.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejections and act favorably upon the claims. If the Examiner requires clarification for any aspect of this response, or if prosecution can be expedited for any other reason, Applicants respectfully request that the Examiner contact the undersigned by telephone.

Respectfully submitted,



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Marked-up Claims

39. (Four times amended) The method as claimed in claim 38 wherein the concentration of water soluble polymer in the liquid medium is 0.3% (weight/volume).
42. (Twice amended) A method as claimed in claim 40 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10% (weight/volume).
- 43 (Amended) A method as claimed in claim 42 wherein the concentration of water soluble polymer in liquid medium is 0.1% (weight/volume).
209. (Amended) The method as claimed in claim 206 wherein the concentration of water soluble polymer in the liquid medium is 0.3% (weight/volume).
212. (Amended) The method as claimed in claim 210 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10% (weight/volume).
213. (Amended) The method as claimed in claim 212 wherein the concentration of water soluble polymer in the liquid medium is 0.1% (weight/volume).

Marked-up Specification

Deleted at page 30 line 20 through page 31, line 27 and inserted at page 4 after line 22:

Figure 1 is an overview of the neurons and transmitters that are known to have a direct influence on the pumping rate of the *C. elegans* pharynx.

Figure 2 shows an example of the detection of enhancers of the pumping rate of the *C. elegans* pharynx, using a fluorescent read-out.

Figure 3 shows an example of the detection of inhibitors of the pumping rate of the *C. elegans* pharynx, using a fluorescent read-out.

Figure 4 shows dose-response curves for the inhibitors tamoxifen, BP554 and pimazide.

Figure 5 shows a dose-response curve for the enhancer clomipramine, showing the toxic effect of DMSO.

Figure 6 shows a dose-response curve for thapsigargin showing the enhancer effect at high concentrations and the inhibitor effect at high concentrations.

Figure 7 illustrates the principle of the movement assay.

Figure 8 illustrates the principles of chemical substrate selection and antagonist selection using the movement screen.

Figure 9 shows the results of a representative movement assay illustrating the change in nematode autofluorescence (y-axis) with time (x-axis).

Figure 10 illustrates the result of an experiment to show the effect of PEG8000 on performance of the pharynx pumping assay. 100 worms (strain HD8) were incubated for 3 hours in the presence of 0.5µM calcein-AM. They were handled with or without the addition of 0.1% PEG.

Figure 11 illustrates the results of experiment to show the effect of viscosity of the medium on performance of the movement assay.

Figure 12 and Figure 13 illustrate the effect of viscosity of the medium on performance of the movement assay for various *C. elegans* mutants in a comparative study. 100 worms were incubated in a round bottom shaped microtiter plate. OD was measured at 340nm in various viscous media (M9, medium viscosity carboxymethylcellulose and high viscosity carboxymethylcellulose). Measurements were done in triplicate.

Figure 14 and Figure 15 illustrate the effect of viscosity of the medium on the pharynx pumping screen. N2 + MC denotes wild-type worms in medium containing carboxymethylcellulose.

Figure 16 and Figure 17 illustrate the kinetics of egg laying assays using N2 worms based on detection of chitinase activity using a fluorescent substrate. The assays were carried out in the presence of varying concentrations of clomipramine and fluoxetine, respectively.

[Figure] Figures 18 to 21 illustrate the effect of compounds of known insecticidal activity on the pharynx pumping rate of *C. elegans*. Fig. 18-Picrotoxin, Fig 19.-Rotenone, Fig 20.-Dieldrin, Fig. 21-Ivermectin. A reduction in the pharynx pumping rate on exposure to insecticide is clearly seen.

At page 4, lines 23-28:

The methods of the invention are all performed in a multi-well plate format and are therefore particularly suitable for use in mid-to-high throughput screening. In a preferred embodiments, the multi-well plates have 96 wells, but the invention is also applicable to multi-well plates with another number of wells, which include but is not restricted to plates with 6, 12, 24, 384, 864, or 1536 wells. The terms “multi-well plate” and “microtiter plate” are used interchangeably [throughout] throughout.

At page 30, lines 18-19:

The invention will be further understood with reference to the following experimental examples together with the accompanying Figures [in which:].